Experimental evaluation of *in vivo* transverse relaxivity of Magnevist in brain tissue

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INTRODUCTION: We experimentally evaluated and compared transverse relaxivity of Magnevist® in grey matter (GM) and white matter (WM) using steady state (SS) *T1* imaging and dynamic susceptibility contrast (DSC) imaging[1,2] with a single contrast injection. SS and DSC are contrast based perfusion techniques that use lathanide paramagnetic agents (such as Gadolinium, Gd) that alter the relaxation - *R1, R2* and/or *R2** of the tissue. The SS approach estimates absolute CBV values based on *T1* changes that occur in the tissue once the contrast agent has equilibrated in the microvasculature. On the other hand, DSC tracks *R2** changes following a rapidly admnistered bolus of contrast during its first pass through the tissue of interest before equilibration. While SS has been successfully used to measure absolute cerebral blood volume (CBV) with high accuracy[3], DSC has been used extensively as well for quantifying cerebral blood flow (CBF), relative CBV and other perfusion parameters. However, DSC measures of CBV rely on the assumption that *R2** changes in the tissue are linearly proportional to the CBV and the relaxivity of Gd (*r2**) is constant and independent of tissue type i.e at any time *t*, $\Delta R2^*(t) = r2^* \bullet [Gd(t)] \bullet$CBV (*[Gd(t)]*= intravascular concentration of Gd in the tissue). It has been shown that this assumption may not necessarily be true and efforts have been made to quantify absolute CBV by calculating correction factors that account for differences in the relaxivity based on micro-vascular architecture, permeability, and proton exchange between the tissue and blood. To assess its variability across different brain regions, we estimated $r2^* \bullet [Gd]_t$ of Magnevist® by comparing the CBV value determined from DSC following a single bolus injection of contrast agent with the CBV value obtained from SS once contrast had equilibrated.

MATERIAL AND METHODS: *Experiment:* 7 healthy subjects were consented under an IRB-approved protocol for a contrast injection study with both SS and DSC methods once they met the appropriate eligibility criteria. Magnevist® (0.1 mmol/kg) was administered through the antecubital vein with 18G needle at 5 ml/s followed by a 40 ml saline flush. First, 2 T1 weighted anatomical images were acquired at the same orientation and resolution as the SS and DSC methods. The imaging protocol for the SS method was as follows: 3D T1 FFE, *TR/TE* = 28/6 ms, FOV = 256 x 256 mm^2, Res = 0.88 x 0.88 x 4 mm^3, slices = 30, SENSE factor = 2.5. Post contrast SS images were acquired approximately 4 min after contrast injection. During the 4 minute interval, DSC data were acquired with *TR/TE* = 1500/54 ms, FOV = 240 x 240 mm^2, resolution = 1.5 x 1.5 x 1.5 mm^3, slices = 15, SENSE factor = 2. 15 baseline images were acquired before contrast injection and 100 during and after contrast injection. In order to preserve the preparation phases of the SS pre-contrast image, 'split-dynamics' were used to insert the DSC scan between the 2 SS scans and one imaging scan protocol was set up for a single contrast injection to measure CBV and *R2** changes with two methods. Both DSC and SS datasets were motion corrected and coregistered to the anatomical images in AFNI[4]. *Analysis*: Absolute CBV was calculated from SS data by subtracting the pre- and post-contrast images and normalizing the difference by a similar difference in voxels of pure blood identified in the sagittal sinus. The concentration time curve for Gd from the DSC method was converted to a curve for $\Delta R2^*$ ($\Delta R2^* = -\ln(S/S_0)/TE$) where S_0 is the baseline signal intensity and S is the signal intensity after injection. The curve was then fit to a gamma variate function given by

$$C(t) = K(t - t_0)^{\alpha} e^{-(t-t_0)/\beta}, t > t_0$$

where K = constant scale factor, t_0 = bolus arrival delay α, β = determine shape of the distribution. Area, A_{R2^*} under the gamma variate curve was computed using $A_{R2^*} = K\beta^{(1+\alpha)}\Gamma(1+\alpha)$. The CBV obtained from the SS method represents the true value with high accuracy, so we can estimate the product $r2^* \bullet [Gd]_t = A_{R2^*}/CBV_{SS}$ where $[Gd]_t = \int [Gd(t)]dt$, assumed to be constant for all tissue. Regions of interests (ROIs) were drawn in the WM, GM, putamen and hippocampus and $r2^* \bullet [Gd]_t$ values were computed and compared across the different ROIs.

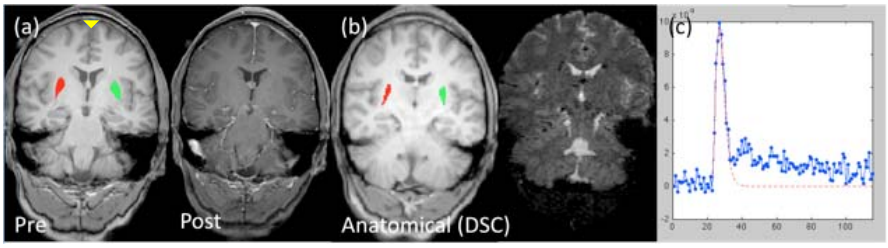

Figure 1*: (a) Pre and post contrast images of SS methods from one subject. Sagittal sinus is shown in yellow and the right and left putamen in red and green. (b) Corresponding anatomical and DSC image (c) DSC ΔR2* curve for the putamen ROI. The blue curve represents the actual data and the red curve represents the gamma variate fit.*

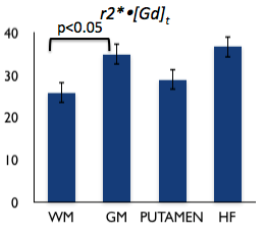

Figure 2*: $r2^* \bullet [Gd]_t$ values in GM tissue and WM for a dose of 0.1 mmol/kg*

RESULTS AND DISCUSSION: ***Figure 1*** shows a representative pre and post contrast image from the SS scan with an ROI in the sagittal sinus and putamen and the corresponding ROIs in the anatomical image for the DSC scan. The DSC $\Delta R2^*$ curve for the putamen ROI is shown in ***Figure 1c***. The average value of $r2^* \bullet [Gd]_t$ in WM, GM, putamen and hippocampus were calculated and are depicted in ***Figure 2***. The $r2^* \bullet [Gd]_t$ values in GM (34.9) and WM (25.8) were significantly different ($p<0.05$). $r2^* \bullet [Gd]_t$ values in different GM regions were not significantly different. With $[Gd]_t$ assumed constant, this study shows that the *r2** values are different for different tissue types. Further, it is likely that the relaxivity of Gd may be different in diseased conditions. CBV measurements estimated with the assumption that the relaxivity of Gd in all tissues is identical should therefore be treated with caution. Accurate estimation of *r2** may be affected by the different resolution in the SS and DSC methods. Also, the imaging data comprised a few slices rather than whole brain coverage. DSC concentration curve may show some regional difference depending on the proximity of the tissue to its perfusing artery. We believe that these variations will not affect the relative difference between *r2** values between the different tissue types.

CONCLUSION: In this study, we estimated experimentally the transverse relaxivity of Gd in the grey and white matter tissues of the brain. Importantly, the relaxivity of Gd (injected at 0. 1 mmol/kg) was found to be signficantly different in different tissues.

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